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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
DUNSTON, JENNIFER ANN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,475	FISHER ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-98* is/are pending in the application.

4a) Of the above claim(s) *4-18,28,29,35-49 and 59-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,19-27,30-34 and 50-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/12/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III (claims 1-3, 19-27, 30-34, and 50-58) in the reply filed on 7/15/2004 is acknowledged. The traversal is on the ground(s) that Groups I-IV are related because they all have the same effect of increasing MDA-5 protein activity. This is not found persuasive because the different inventions of Groups I-IV have different mechanisms (i.e. modes of operation) of protecting a subject against a viral infection: by administration of MDA-5 protein directly (Group I), a nucleic acid capable of expressing MDA-5 protein (Group II), an agent that increases the activity of an mda-5 promoter (Group III), and an agent that acts on MDA- 5 protein to increase the functional activity of the protein (Group IV).

Further, it is acknowledged that claim 1 links inventions of Groups I-IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim, claim 1. Upon the allowance of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01 .

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-98 are pending in the instant application. Claims 4-18, 28, 29, 35-49 and 59-98 are withdrawn from consideration as being drawn to a nonelected embodiment. An examination on the merits of claims 1-3, 19-27, 30-34, and 50-58 follows.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for claims 1-3, 19-27, 30-34 and 50-58 of this application. The parent applications do not provide support for the administration of agents to a subject wherein the level of MDA-5 protein activity is increased such that the subjected is protected from viral infection or the infection is limited. Claims 1-3, 19-27, 30-34 and 50-58 are assigned an effective filing date of 1/22/2002.

Information Disclosure Statement

Receipt of an information disclosure statement, filed on 5/12/2003, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

Drawings

The drawings are objected to because of the following reasons:

(i) Figure 4 is not legible and will not reproduce well. The letters "PNAS" are obscuring the last row of the alignment;

(ii) The localization of GFP-MDA5 is not visible in Figure 6B; and

(iii) The bands corresponding to purified proteins cannot be seen in Figure 8A.

Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Marked-up Drawings" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

Specification

The disclosure is objected to because of the following informalities: roman numerals (i) and (ii) appear to be missing in paragraph [0038] (page 16), the number 23 appears twice in the list of viruses (page 27), and page 39 appears to have a typographical error (IFN-5, paragraph [0089]).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 19-27, 30-34 and 50-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 32 are vague and indefinite in that the metes and bounds of the term "effective amount" are unclear. It is unclear whether there is *necessarily* a link between increased MDA-5 activity and protecting a subject against viral infection (claim 1) or limiting viral infection in a subject (claim 32). The "effective amount" of an agent can refer to the amount required for increased MDA-5 activity and/or the amount required to protect against or limit viral infection in a subject. Further, it is unclear whether the increased MDA-5 activity is merely observed upon administration of the agent, or increased MDA-5 activity results in

protecting against or limiting viral infection. It would be remedial to amend the claim to indicate to what the "effective amount" refers.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The elected claims are drawn to a method of protecting a subject against viral infection or limiting viral infection is a subject, wherein the agent increases the activity of the *mda-5* promoter. The positive method step is "administering, to the subject, an effective amount of an agent." The claim is interpreted such that the effective amount refers to the amount of an agent that is required to increase MDA-5 activity, and the increase in MDA-5 activity results in the protecting or limiting effect with regard to viral infection in a subject (see the 112, second paragraph, rejection above).

Claims 1-3, 19-27, 30-34 and 50-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of

experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Breadth of the claims and nature of the invention: The claims are drawn to a method of protecting a subject against viral infection (claims 1-3, 19-27 and 30-31) or limiting viral infection in a subject (claims 32-34 and 50-58). The positive method step is "administering, to the subject, an effective amount of an agent," wherein the agent increases the activity of the *mda-5* promoter, resulting in increased MDA-5 protein activity.

Claims 1-3, 19, 22, 25, 30-34, 50, 53 and 56 are broad in that the claims encompass any agent. The claims do not specify any structural characteristics of the agent. Claims 20, 23, 54 and 51 are narrower in scope in that the claims specify the administration of TNF-α to the subject. Claims 21, 24, 55 and 52 specify the administration of poly(I)(C) to the subject. Claims 26 and 57 specify the administration of interferon to the subject, and claims 27 and 58 further limit the interferon to β-interferon (IFN-β). Further, the claims encompass an infection by any virus. Claims 2 and 33 broadly categorize the virus as one that produces a viral helicase. Claims 3 and 34 broadly categorize the virus as one that does not produce a viral helicase. Moreover, all claims are broad in that the "effective amount" of the agent is not specified, and the subject can be any individual from any patient population (human or otherwise).

Guidance of the specification and existence of working examples: The specification envisions the use of agents such as interferon alpha, interferon beta, interferon gamma, tumor necrosis factor alpha and poly IC to increase transcription of the endogenous *mda-5* gene (e.g. page 24, paragraph [0058]). The specification provides examples of viruses which may be treated, including viruses such as picornoaviruses, caliciviruses, birnaviruses, retroviruses,

hepadneaviruses, circoviruses, parvoviruses, papoviruses, adenoviruses, herpesviruses, poxviruses, iridovirus family members, arboviruses, and unclassified human and animal viruses including Borna Disease virus, hepatitis E and X viruses (e.g. pages 25-28, paragraph [0062]). Examples of viruses which encode helicase molecules are described in the specification as the following: poxviuses such as vaccinia, alphaviruses such as Semliki Forest virus (SFV), flaviviruses such as hepatitis C virus (HCV), reoviruses such as rotaviruses A and B, and picornaviruses such as poiovirus, among others (e.g. page 28, paragraph [0063]).

The working examples of the specification are limited to *in vitro* analysis of *mda-5* gene expression. The specification teaches the effect of the following agents on the levels of *mda-5* transcript in HO-1 human melanoma cells: MEZ, IFN-β, MEZ and IFN-β, IFN-γ, MEZ and IFN-γ, all-trans retinoic acid, mycophenolic acid (RA), 12-O-tetradecanoylphobol-13-acetate (TPA), cAMP, 8-bromo-3'-5' cyclic adenosine monophosphate (8-Br-cAMP), methyl methanesulfonate (MMS), IFN-α, IFN-μ, IL-6, epidermal growth factor (EGF), transforming growth factor-α (TGF-α), transforming growth factor-β, TNF-α, and platelet-derived growth factor (PDGF). Of these agents, it appears that only IFN-γ was tested at different amounts (100 units/ml and 1,000 units/ml) (e.g. Figure 5A and Figure 5B). Though each of these reagents were tested, the specification teaches that **only** the IFNs (α, β, and γ) and TNF-α significantly increased steady-state *mda-5* transcript levels within 24 h (e.g. page 38, paragraph [0087]). Thus, the specification teaches the unpredictable nature of *mda-5* promoter activity in response to a variety of agents. The only other increase in *mda-5* expression resulted from the combination of MEZ with IFN-β or IFN-γ (e.g. page 38, paragraph [0087]). The induction of *mda-5* expression was confirmed in cancer and normal cell lines of various sources (e.g. page 39, paragraph [0088]).

Only a subset of agents tested *in vitro* resulted in a significant increase in *mda-5* promoter activity as measured by Northern blotting. There are no teachings in the instant specification of the effect of any agent on the progression any viral infection *in vitro* or *in vivo*. The specification does not provide guidance with regard to an "effective amount" of any agent in terms of protecting a subject (human or otherwise) from viral infection or limiting viral infection in a subject. Though applicants assert that the response of cells *in vitro* to IFN treatment "strongly suggests that *mda-5* plays a critical role in responses that are specific for IFN signaling such as antiviral effect …", there is no convincing evidence of record to indicate that the induction of *mda-5* expression *in vitro* is mechanistically linked to a protective effect against viral infection in a subject.

Predictability and state of the art: At the time of filing, the art of increasing MDA-5 activity to protect a subject against viral infection or limit viral infection in a subject was underdeveloped. There is no prior art to indicate the "effective amount" of an agent capable of increasing *mda-5* expression in a subject (human or otherwise) or of an agent capable of increasing *mda-5* expression such that one is protected from viral infection.

At the time of filing the specific agents recited in the claims (interferon, IFN-β, TNF-α and poly IC) were known to be important regulators of the antiviral response *in vivo*. Interferons are antiviral proteins released by animal cells in response to a viral infection (Levy, US Patent No. 3,952,097; e.g. column 1, lines 17-18). Further, natural and double-stranded synthetic RNA stimulate the production and secretion of interferons from animal cells (Levy, e.g. column 1, lines 18-37). It is now known that more than 100 cellular genes are transcriptionally stimulated after interferon α/β mediated activation of cellular signaling (Garcia-Sastre, Microbes and

Infection, Vol. 4, pages 647-655, 2002; e.g. page 648, paragraph bridging columns). Further, tumor necrosis factors are major components of the immune system involved in the control of viral infection *via* direct antiviral activity (Herbein et al, P.S.E.B.M. Vol. 223, pages 241-257, 2000; e.g. page 252, Conclusion).

Although the antiviral effects of the interferons, TNF-α and poly IC were well known in the art at the time of filing, the nature of the effect of the agent on cells containing virus was known to be unpredictable due to the ability of viruses to evade the host immune response. For example, several viruses commandeer the immune defense by interacting directly with the TNF pathway to favor the proliferation of infected cells, by producing viral decoy proteins that will bind to TNF to diminish its antiviral effect, or by triggering the killing of either infected cells to select for malignant cells or uninfected bystander T cells to exhaust the immune system (Herbin, page 252, Conclusion; Table I; Table II). Further, Garcia-Sastre teaches that viruses have "learned" different ways to inhibit the interferon α/β system, by inhibiting either interferon α/β production, interferon α/β signaling, or the antiviral activity of interferon α/β-induced proteins (e.g. page 649, section 2; Table 1). Further, the "effective amount" of an agent is also unpredictable. As noted by Tovey:

> "It is widely considered that in order to obtain the maximum therapeutic effect, the highest possible dose of interferon should be used. Although the availability of recombinant material has meant that very high dose levels are feasible, in practice it has been found that the side-effects of interferon administration have severely limited the dose of interferon which can be used and the duration of treatment. These side-effects include severe malaise and depression, leading in some cases even to suicide." (See column 1, lines 59-67)

The toxicity of these agents is not limited to the interferons. For example, Morahan et al

(PNAS, Vol. 69, pages 842-846, 1972) teach the toxicity of poly IC in that it produces

effects similar to that of endotoxin: it is pyrogenic, may elicit leukopenia, and can provoke the Schwartzman phenomenon (i.e. toxic shock).

The post-filing art provides further support for the unpredictable nature of antiviral therapy. Cocude et al (Journal of General Biology, Vol. 84, pages 3215-3225, 2003) identified an RNA helicase referred to as RH116 (a.k.a. MDA-5 and Helicard) as a gene whose expression was downregulated upon Murabutide treatment of HIV-1 infected cells (e.g. e.g. paragraphs bridging pages 3215-3216 and 3221-3222). Cocude et al demonstrate that overexpression of RH116 results in an inhibition of cell growth, upregulation of HIV-1 replication, and an increase in the level of viral transcripts in HIV-1 infected HeLa-CD4 cells (e.g. Figure 4; Figure 6; page 3223, bridging paragraph). Further, Cocude et al demonstrate a shift in the cellular localization of RH116 from cytoplasmic to nuclear upon HIV-1 infection of cells (e.g. page 3218, Detection and localization of RH116; page 3221, right column, second paragraph). Moreover, HIV-1 infection induced an increase in the levels of RH116 transcript and protein (e.g. paragraph bridging pages 3220-3221). Contrary to the claimed invention of the instant application, Cocude et al suggest that RH116 is implicated in the positive regulation of HIV-1 replication, thus drugs that block RH116 function may be useful therapeutics for HIV-1 treatment (e.g. page 3224, left column, last paragraph).

Amount of experimentation necessary: In order to practice the claimed invention, one of ordinary skill in the art would have to first envision a subject from a patient population at risk for infection by a specific virus. One would then have to identify candidate agents that increase the expression of MDA-5 protein by acting on the *mda-5* promoter. One would then have to experimentally determine a safe dose for the agent. Following that, one of skill in the art would

have to determine if the dose of the agent was sufficient to increase the level of transcription from the *mda-5* promoter and protect the subject against infection by the specific virus or limit the infection.

If unsuccessful in the first attempt, which is likely given the complexity of the therapeutic administration of immunomodulatory agents and the lack of guidance from the specification, one of skill in the art would have to envision a modification of the first approach (e.g. the dose, timing of administration) or an entirely new approach (e.g. a different agent). If unsuccessful again, which is likely given the unpredictability of the art, one would have to repeat the entire unpredictable process until successful.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed methods of protecting a subject against viral infection or limiting viral infection in a subject. Thus, the invention of claims 1-3, 19-27, 30-34 and 50-58 is not considered to be enabled by the instant specification.

Claims 1-3, 19, 22, 25, 30-34, 50, 53 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 19, 22, 25, 30-34, 50, 53 and 56 are drawn to a method of protecting a subject against viral infection (claims 1-3, 19-27 and 30-31) or limiting viral infection in a subject (claims 32-34 and 50-58). The positive method step is "administering, to the subject, an effective amount of an agent," wherein the agent increases the activity of the *mda-5* promoter, resulting in increased MDA-5 protein activity.

Thus the rejected claims comprise a set of agents administered at an "effective amount" to protect a subject from viral infection or limit viral infection in a subject. The virus can be any virus that can infect any subject (human or otherwise). The set of agents must act on the *mda-5* promoter to increase the level of MDA-5 activity. Thus, the rejected claims encompass an incredibly enormous genus of agents that must meet specific functional limitations (i.e. an effective amount of the agent must increase MDA-5 activity and protect against or limit viral infection in a subject). Each of the different agents is likely to have a different "effective amount". Further, the "effective amount" may vary depending upon the immune status of the subject being treated, the type of viral infection, or both. Given that the range of agents administered at an "effective amount" encompassed by the instant claims is any that is biologically possible, and that the claims encompass any virus that infects any subject, the genus of agents encompassed by the rejected claims is so broad as to be incalculable.

The specification envisions the use of agents such as interferon alpha, interferon beta, interferon gamma, tumor necrosis factor alpha and poly IC to increase transcription of the endogenous *mda-5* gene (e.g. page 24, paragraph [0058]). The specification provides examples of viruses, which include virtually any known virus (e.g. page 28, paragraph [0063]). There is no description in the specification as originally filed of any effective amount of an agent that

would meet the claim limitations for any virus in any organism. While the IFNs (α, β, and γ) and TNF-α significantly increased steady-state *mda-5* transcript levels *in vitro*, there is no evidence that these agents could be administered to a subject to increase MDA-5 activity, resulting in protecting against or limiting viral infection.

Even if one accepts that the examples described in the specification are capable of increasing the level of MDA-5 activity in a cell *in vitro*, the examples are only representative of a cell culture system into which no virus has been introduced.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of agents and the effective amounts of those agents that increase the activity of the MDA-5 protein by acting upon the *mda-5* promoter such that protecting from or limiting a viral infection is achieved in a subject.

Thus, there is no structural/functional basis provided by the prior art or instant specification for on e of skill in the art to envision an effective amount of any agent that is capable of increasing *mda-5* transcription and either protecting a subject from viral infection or limiting viral infection in a subject. Therefore, one of skill in the art would not have been able to envision a representative number of agents and effective amounts sufficient to describe the broad genus of agents encompassed by the rejected claims. One of skill in the art would thus have reasonably concluded applicants were not in possession of the claimed invention for claims 1-3, 19, 22, 25, 30-34, 50, 53 and 56.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The elected claims are drawn to a method of protecting a subject against viral infection or limiting viral infection is a subject, wherein the agent increases the activity of the *mda-5* promoter. The positive method step is "administering, to the subject, an effective amount of an agent." The claim is interpreted such that the effective amount refers to the amount of an agent that is required to protect a subject against viral infection or limit viral infection in a subject. (see the 112, second paragraph, rejection above). Further, the additional limitation of claims 19, 22, 25, 50, 53 and 56, which recite "wherein the agent increases the activity of an *mda-5* promoter" is interpreted as limiting the agent to one that is capable of activating transcription from the *mda-5* promoter.

Claims 1, 2, 19, 21, 22, 24, 32, 33, 50, 52, 53 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Richmond et al (PNAS, Vol. 64, pages 81-86, 1969; see the entire reference).

Richmond et al teach the administration of poly IC to mice by injection during a period extending from 48 hours before to 18 hours after foot-and-mouth disease virus (FMDV) inoculation (e.g. page 82, *Materials and Methods* and *Course of host resistance*). Richmond et al observed 100% survival of mice challenged with FMDV when poly IC was injected 18 hours before the virus, whereas untreated mice did not survive (e.g. page 83, paragraph 1; Figure 1).

Claims 1, 2, 19, 20, 22, 23, 32, 33, 50, 51, 53 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Rossol-Voth et al (Journal of General Virology, Vol. 72, pages 143-147, 1991; see the entire reference).

Rossol-Voth teach the administration, to mice, of 10 ng or 100 ng of TNF-α 8 hours after infection with herpes simplex virus type 1 (HSV-1). As a result of treatment, 80% of the mice treated with 100 ng of TNF-α and 60% of mice treated with 10 ng of TNF-α survived more than 2 weeks as compared to untreated mice which were all dead by 2 weeks (e.g. page 144, bridging paragraph; Figure 1).

Claims 1, 3, 19, 25-27, 30-32, 34, 50 and 56-58 are rejected under 35 U.S.C. 102(e) as being anticipated by Tovey (US Patent No. 6,207,145; see the entire reference).

Tovey teaches the administration, to mice, of 10,000 IU of a mixture of interferon-α and interferon-β once a day for 4 days beginning 7 hours after Vesicular Stomatitis virus (VSV) infection. As a result of treatment, 30% of the mice live to 21 days as compared to untreated mice who all die by 10 days (e.g. column 13, Example 4).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
Art Unit 1636

jad

GERRY LEFFERS
PRIMARY EXAMINER